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10/595,275	04/04/2006	Masaya Nakatani	2006-0239A	6597
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EXAMINER				
KASTEN, ROBERT J				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/595,275

Applicant(s)

NAKATANI ET AL.

Examiner

ROBERT KASTEN

Art Unit

4191

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 April 2006.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 and 7-33 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1-5 and 7-33 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
10) ☒ The drawing(s) filed on 04 April 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/S508)
Paper No(s)/Mail Date 4/4/2006
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

Summary

1. This is a first and non-final action on the merits.
2. Claim 6 was cancelled by preliminary amendment, 4/4/2006. Claims 1-5 and 7-33 are pending.

Specification

3. The disclosure is objected to because of the following informalities: page 16, lines 4-6 "Molded plate 502A previously molded is stuck on molded plate 502B previously molded, thus providing plate 502 of complexity." In page 17, paragraph 2, multiple "communicatings" should be "communicates." etc.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
5. Claim 1 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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6. Claim 1, line 21 recites the limitation "the second flow passage" in the probe for measuring the electric potential of a cell. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-5, 10, 13-15, 17 are rejected under 35 U.S.C. 102(b) as being anticipated by BECH et al (2002/0063067), from here on in referred to as BECH.

a. BECH teaches a microfluidics device used in a system for making electrophysiological measurements, which is essentially probe as referenced in the claimed invention. MPEP 2111.02 [R-3] states that the effect of the preamble must be taken on a case by case basis. In part II of this chapter, if "the preamble merely states, for example, the purpose of intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction," as is the case here. The claims rejected herein only require structural limitations of the probe. The preamble has not been given patentable weight.

b. Specifically, Claims 1-5, 13-14 are anticipated by Figures 7A and 8 in BECH. Figure 7A is a blown-up representation of 74 on Figure 8.

c. Concerning Claim 1, Figure 8 shows a device with a plate 60 with an upper surface (not defined by number), the plate having a first cavity 78 and 77 provided in the surface, a second cavity 82 which is in the bottom of 78 and 77. A first flow passage is provided which connects 81 with cavity 82 with the first opening occurring at 81 and the outside of the plate and the second opening occurring at 82. Cavity 78 has a bottom surface (not identified by number) which communicates with 77. Figure 8 also teaches a sensor element 74 provided in the cavity created by 78 and 77, which is further detailed in Figure 7A. This sensor element has a thin plate 75 with a first surface and a second surface (not defined by number) which has a plurality of through-holes 76 provided therein. These through-holes have a first opening and a second opening and communication between the two openings. Thin plate 74 separates cavity 78/77 and 82, and allows communication between 82 and the second opening of 76. Figure 8 also teaches a supporting substrate (not identified by number) under 77/78 and extending next to reservoirs 79 and 81. The first flow passage connects 82 with 81, which is an electroosmotic pump, analogous to the claimed sucking device and allows for fluid flow in the first flow passage. A second flow passage connects 82 with 79, which is

an electroosmotic pump in the bottom of a reservoir which is suited to hold any fluid.

d. Concerning Claim 2, Figure 8 shows how thin plate 75 sits flush with the rest of sensor element 74 which is integrally connected with the rest of the substrate, and therefor constitutes the bottom of cavity 77. Therefore, this claim is rejected because the second surface of thin plate 75 is flush with the bottom surface of 77, which is 74.

e. Concerning Claim 3, the surfaces of the supporting substrate (not identified by number) referred to in the rejection of claim 1 are presented in identical fashion to the claimed invention in Figure 8, with the bottom of the first cavity established with the surface of the supporting substrate.

f. Concerning Claim 4, BECH refers to this embodiment as having "housing 60," which contain these flow paths. Even though "plate" and "substrate" are never explicitly defined, the housing 60 can be considered the complexing of all structural elements, meaning that the plate analogues around above 77 and the substrate analogues around 78 and 82 can be considered bonded together, possible by the use of adhesive like in 69 of 7A.

- g. Concerning Claim 5, Figure 8 teaches a second flow path connecting 81 with 82 in which the first opening allows flow to 82 and second opening opens to 81 and the outside of the plate.
- h. Concerning Claim 13, BECH teaches Figure 7A, which shows two electrodes 63 and 64 positioned around the first and second openings of the through-holes 76.
- i. Concerning Claim 14, Figure 7A shows how the legs of 74 create a pocket on the side encompassing the second openings of the through-holes 76.
- j. Concerning Claim 15, page 3, paragraph 0022 discloses that the "first canal" may be made of glass. Though BECH does not stipulate the composition of the rest of the device, the easiest way to make the first whole device out of glass, which would allow for the transmittance of light in the whole device.
- k. Concerning Claims 10 and 17, figure 8 shows a bump formed in the bottom of cavity 82 which corresponds to the bump 17 in cavity 6, while still containing the limitations of Claim 1 and Claim 5 where applicable.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claim 7 rejected under 35 U.S.C. 103(a) as being unpatentable over BECH in light of ROTTER et al (US 2,366,654), from here on in referenced as ROTTER.

a. BECH teaches a microfluidics device in Figure 8 with the limitations of claim 1 (see 102 (b) rejection above).

i. BECH does not expressly disclose a valve between the reservoirs and flow passages and his device.

ii. However, ROTTER discloses claim 1, which is a pump containing multiple valves.

iii. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the pump of BECH to include a valve such as any found in ROTTER or the like. While a pump does not necessitate the use of a valve, the concept of pairing a valve with a pump is not novel, and therefore the claimed invention is obvious.

12. Claims 8, 11, 16, 18-19 rejected under 35 U.S.C 103(a) as being unpatentable over BECH in view of FISHMAN al (2003/0032946), from here on in referenced as FISHMAN.

a. Concerning Claims 8 and 11, BECH discloses Figure 8, a microfluidics device for use in making electrophysiological measurements with all the limitations of Claims 1 and 5 (see 102 (b) rejection rationale above).

i. BECH does not appear expressly disclose that the flow passages be greater than 0.01mm^2 in cross-sectional area.

ii. However, FISHMAN discloses Figures 7A and 7B, which bare a large strong resemblance to the claimed invention as well as BECH, with flow passages 80 and 82 communicating with cavities 78 and 36 and an aperture 24 which can contain a membrane 42 (Figure 4).

iii. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the features of

BECH with the features of FISHMAN. FISHMAN's features are analogous to the flow chambers, cavities, and sensor element found in BECH, but stipulate that these flow passages each be capable of accepting "24 gauge Teflon hoses" (page 13, paragraph 0120). 24 gauge is equivalent in size to a diameter of .58 mm, which yields a cross-sectional area greater than the claimed .01mm². Thus, the larger flow passages than those described in BECH are obvious.

- b. Concerning Claim 16, BECH discloses a Figure 8, a microfluidics device with all the limitations of Claim 1 (see the 102(b) rejection above).
 - i. BECH does not appear to expressly disclose that the thin plate of the sensor element be capable of transmitting visible light.
 - ii. However, FISHMAN discloses a device which can be monitored using confocal microscopy (page 13, paragraph 0118, lines 6-7). This is a test that necessitates a translucent device or surface, (see US 3,013,467 Figure 1D).
 - iii. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the thin plate of BECH to include the translucency of FISHMAN because BECH would benefit greatly from being to monitor the effectiveness of the other major features of his invention, namely the ability to manipulate cells for the purposes of patch clamping.

c. Concerning Claim 18, BECH discloses a Figure 8, a microfluidics device for use in making electrophysiological measurements with all the limitations of Claim 1 (see 102(b) rejection rationale above).

i. BECH does not appear to expressly disclose that the first flow surface of the thin plate of the sensor element 74 be flush with plate.

ii. However, FISHMAN discloses figure 1C, which shows layer 16 flush with layer 18.

iii. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the sensor element with FISHMAN as this configuration is obvious to try. There are only so many possible configurations of the thin plate on the plate and this configuration, especially since one similar had been tried prior, would be an obvious design choice at any stage of development for its possible implications with respect experimental results and manufacturing ease.

d. Concerning Claim 19, BECH discloses a Figure 8, a microfluidics device for use in making electrophysiological measurements with all the limitations of Claim 1 (see 102(b) rejection rationale above), as well as the orientation of the plates which are evident from the parallel orientation of the components in that figure. BECH also discloses feature 14, a cavity in layer 12, a portion of thin plate 74 from Figure 7A, which reads on the claimed third cavity.

- i. BECH does not appear to expressly disclose the limitations of Claim 18, which is required in the dependency on Claim 19 on Claim 18. BECH also does not appear to expressly disclose the limitation of the third cavity with is provided in the thin plate.
- ii. However, FISHMAN discloses all the limitations of Claim 18 (see 103(a) rationale above)

13. Claims 9,12 rejected under 35 U.S.C. 103(a) as being unpatentable over BECH in light of TAYLOR et al ("...Turbulence in Curved Pipes," *Proceedings of the Royal Society of London*, 1929), from here on in referenced as TAYLOR.

- a. BECH discloses a microfluidics device with all the limitations of claims 1 and 5 (see the 102 (b) rejections above), in this case specifically the flow passages.

- i. BECH does not expressly disclose the shape of the flow passages, which appear to only be straight.
- ii. However, TAYLOR discloses in a summary on page 1 of his publication that "a higher speed of flow is necessary to maintain turbulence in a curved pipe than in a straight one."
- iii. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the straight flow path of BECH with a curved flow path, since curved flow paths were shown in TAYLOR to increase the flow velocity required for turbulent flow. One of ordinary skill in the art would have sought to

avoid turbulent flow in this case, since turbulent flow can create bubbles in the flow passages which, apart from possibly causing blockages in the passages, have been shown to be detrimental to similar electrical cellular experiments (e.g. electroporation) due to the possibly of "arcing" in the sample. Arcing can lead to a decrease in cellular viability and may cause loss of the sample.

<<http://userpages.umbc.edu/~jwolf/m7.htm>>

14. Claims 20-33 rejected under 35 U.S.C. 103(a) as being unpatentable over BECH in light of JOLLEY et al (US 4,704,255), from here on in referred to as JOLLEY.

- a. Concerning Claim 20, BECH teaches all the limitations of claim 1.
 - i. BECH does not appear to expressly disclose a well array.
 - ii. However, JOLLEY discloses an array of connected wells in figure 4.
 - iii. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the microfluidics device of BECH to include the array of wells present in JOLLEY. The claimed invention in this case is simply a multiplication of the device claimed in claim 1. Since claim 20 essentially just requires a plurality of claim 1, the fact that JOLLEY has disclosed a device with a plurality of wells resembling those in claim 1 but lacking key

features in BECH leads to the conclusion that an array of the initial, rejected invention is not in and of itself which teaches an array of connected wells.

b. Concerning Claim 21, BECH discloses a microfluidics device with all of the limitations of claim 1.

i. BECH does not appear to expressly disclose the limits of claim 20 or the well walls with tapered sides.

ii. However, JOLLEY discloses an array of connected wells with tapered sides in the wells shown in figure 7. The formation of the wells into this shape is therefore an obvious variation on the original claimed invention 1.

iii. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the reservoirs of BECH with the tapered wells of JOLLEY using an obvious to try rationale. Two major well formations are the strict cylindrical form like in BECH or the tapered form as in JOLLEY, with each form having well established pros and cons. Therefore it would have been obvious to substitute one type of well for another.

c. Concerning Claim 22, BECH discloses a microfluidics device with all the limitations of claim 1 as well as the presence of electrodes in the device in figure 7A, parts 63 and 64.

- i. BECH does not appear to expressly disclose the limits of claim 20.
 - ii. However, JOLLEY discloses the limits of claim 20 (see above). The *prima facie* case of obviousness can be seen above.
- d. Concerning Claim 23, BECH discloses a microfluidics device with all the limitations of claim 1 as well as the use of said device as claimed in claim 23 in figure 8, with 79 holding fluid, 78 holding cellular fluid, and sucking devices (electromotive pumps) pulling both fluids.
 - i. BECH does not appear to expressly disclose the limits of claim 20.
 - ii. However, JOLLEY discloses the limits of claim 20 (see above.) The *prima facie* case of obviousness can be seen above.
- e. Concerning Claim 24, BECH discloses a microfluidics device with all the limitations of claim 1.
 - i. BECH does not appear to expressly disclose the limits of claim 20, nor does it appear to disclose where the second well is positioned.
 - ii. However, JOLLEY discloses the limits of claim 20 (see above). The *prima facie* case of obviousness can be seen above.
 - iii. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the location of

the second well with the location inherent in that of JOLLEY. The orientation of the well in relation to the thin plate is obvious from claim 20, which stipulates that the well must be in communication with the through-hole in the thin plate. One of ordinary skill in the art would have placed the well in that position, as it is the position that affords the least complexity, both in terms of fabrication and eventual implementation in laboratory experiments.

f. Concerning Claim 25, BECH discloses a microfluidics device with all the limitations of claim 1, as well as feature 77 in figure 8, which can be construed as the claimed well, which is certainly bigger than the sensor element, which can be construed as feature 74.

i. BECH does not appear to expressly disclose the limits of claim 20, nor are those features mentioned above identical to the claimed features.

ii. However, JOLLEY discloses the limits of claim 20. The prime facie case of obviousness can be seen above. Also, the relative size of features 77 and 74 in BECH and the claimed relative sizes rejected herein are essentially identical or at least similar enough to be structurally and functionally obvious variants of one another.

g. Concerning Claim 26-27, BECH discloses a microfluidics device with all the limitations of claim 1, as well as figure 8 with features 79 and 81, which are wells having larger diameters than their through-holes, and therefore anticipate the requirement of being larger than the second openings in the flow passages claimed herein.

i. BECH does not appear to expressly disclose the limits of claim 20.

ii. However, JOLLEY discloses the limits of claim 20 (see above). The prime facie case of obviousness can be seen above.

h. Concerning Claim 28, BECH discloses a microfluidics device with all the limitations of claim 1, as well as figure 8 with features 77, 79, and 81, which are analogous to the wells claimed herein as they have through-holes as well as a planar arrangement.

i. BECH does not appear to expressly disclose the limits of claim 20.

ii. However, JOLLEY discloses the limits of claim 20 (see above). The prime facie case of obviousness can be seen above.

i. Concerning Claim 29, BECH discloses a microfluidics device with all the limitations of claim 1.

- i. BECH does not appear to expressly disclose the limits of claim 20, nor does it expressly disclose homogeneity of fabrication materials.
 - ii. However, JOLLEY discloses the limits of claim 20 (see above). The prime facie case of obviousness can be seen above. JOLLEY also teaches that most all parts can be made of plastic (column 3, paragraph 7).
 - iii. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art that homogeneity of materials was an option during fabrication.
- j. Concerning Claims 30-32, BECH discloses a microfluidics device with all the limitations of claim 1, as well as possible fabrication materials such as "silicon, plastics, pure silica and other glasses such as quarts and Pyrex or silica doped with one or more dopants selected from the group of Be, Mg, Ca, B, Al, Ga, Ge, N, P, As and oxides from any of these. Correspondingly, the substrate itself can consist of any of these materials (page 7, paragraph 0106, lines 5-10)."
- i. BECH does not appear to expressly disclose the limits of claim 20.
 - ii. However, JOLLEY discloses the limits of claim 20 (see above). The prime facie case of obviousness can be seen above.

k. Concerning Claim 33, BECH discloses a microfluidics device with all the limitations of claim 1.

i. BECH does not appear to expressly disclose the limits of claim 20, nor does it expressly disclose an array of wells.

ii. However, JOLLEY discloses the limits of claim 20 (see above). The prime facie case of obviousness can be seen above. JOLLEY also discloses an array of wells.

iii. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the single device in claim 1 as anticipated by BECH to include the array of wells of JOLLEY, as high-throughput is always a goal and a plurality of wells has been used to solve this problem in multiple area of research including cellular fluorescence assays, protein concentration assays, protein activity assays, etc.

Conclusion

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT KASTEN whose telephone number is (571)270-7598. The examiner can normally be reached on Mon-Thurs, 8am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Barbara Gilliam can be reached on 571-272-1330. The

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fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ROBERT KASTEN/
Examiner, Art Unit 4191

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